Remarks

Claims 2, 4-7, 9, 11, 38-54, 62, 118 and 120 were considered in the Office action of July 26, 2001. Certain of the claims were rejected under 35 U.S.C. § 112, first paragraph. Claim 4 was rejected under 35 U.S.C. § 112, second paragraph. In addition, certain of the claims were rejected under 35 U.S.C. §102 over Hillier et al., (1995). Finally, claims 40, 41 and 46-49 were allowed. Applicants address the rejections below inasmuch as they may apply to the claims as amended.

1. The Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 2, 4, 9, 11 and 45 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors were in possession of the invention at the time that the application was filed. Specifically, the term "variant" was said to fail to convey a common structural attribute defining the claimed members of the genus. Applicants have amended the claims to recite that the protein corresponding to the claimed variant exhibits guanine nucleotide exchange factor activity in an *in vitro* assay. According to the "Guidelines for the Examination of Patent Applications Under 35 U.S.C. 112, "Written Description" Requirement", Federal Register, Vol. 66, No. 4, pages 1099-1111, (January 5, 2001), the written description requirement for a claimed genus may be satisfied through disclosure of functional characteristics coupled with a known or disclosed correlation between function and structure (see page 1106). Applicants' claims, as amended, recite variants that function such that specific biological activity is exhibited. That function is directly correlated to the primary structure, and resulting secondary and tertiary structures of the corresponding variant protein, as disclosed in the specification at page 21, lines 10 and 11, and in Example 2, starting on page 54. As such, Applicants respectfully submit that the written description requirement has been satisfied by the disclosure in the specification of functional characteristics that are coupled with a known and disclosed correlation between the function and structure of the claimed members of the genus. Accordingly, Applicants respectfully submit that the claims, as amended, are sufficiently described in the specification.

Claims 42-45, 50-54 and 62 were said to contain subject matter that was not described in the specification in such a way so as to enable one skilled in the art to make or use the invention. Specifically, the claims were said to cover gene therapy, which was said to not be enabled in the specification. Applicants have amended the claims to recite a host cell "in culture." Applicants respectfully submit that methods of preparing and maintaining such a host cell in culture are well known in the art (see page 30, lines 10-14 of the specification), and that no undue experimentation would be required to practice the invention as claimed in the claims, as amended. As such, Applicants respectfully submit that those claims are enabled in the specification.

Finally, claims 118 and 120 were said to contain subject matter that was not described and/or enabled in the specification. Claims 118 and 120 have been canceled, thereby obviating the rejections with respect to those claims.

For the reasons discussed above, Applicants respectfully request that the rejections under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

2. The Rejections Under 35 U.S.C. § 112, Second Paragraph

Claim 4 was rejected as being indefinite in the recitation of "stringent hybridization conditions." Applicants respectfully submit that the term is known within the art, and is defined in the specification at pages 18 and 19. Nevertheless, Applicants have amended claim 4 to recite stringent hybridization conditions that comprise a temperature and an ionic strength that are within specific ranges. As such, Applicants respectfully submit that this rejection should be reconsidered and withdrawn.

3. The Rejection Under 35 U.S.C. § 102

Claims 5-7 were rejected under 35 U.S.C. § 102 over Hillier et al. (1995). Anticipation under 35 U.S.C. §102 requires that a single reference teach each and every element of a claim. Verdegaal Bros. v. Union Oil Co. of California, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Hillier et al. report nucleotide regions said to correspond to nucleotides 2594-3009 of SEQ ID. NO. 17. Claims 5-7, as previously amended, recite consecutive nucleotides of specific regions of

the claimed sequence which are, at least in part, outside of the region taught by Hillier et al. As such, Hillier et al. fails to disclose each and every element of any of claims 5-7. Accordingly, Applicants respectfully submit that Hillier et al. does not anticipate those claims under 35 U.S.C. § 102, and that the rejection thereunder should be reconsidered and withdrawn.

Conclusion

Applicants respectfully submit that the claims are now in condition for allowance. If the Examiner believes that a conversation with Applicants' attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at the telephone number below.

Respectfully submitted,

12/26/01
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CLAIM AMENDMENTS IN MARK-UP FORMAT

2. (Twice Amended) An isolated nucleic acid comprising a nucleotide sequence encoding a protein selected from the group consisting of an hcAMP-GEFII protein having the amino acid sequence of SEQ ID NO: 18, a normal variant of said hcAMP-GEFII protein, and a mutant of said hcAMP-GEFII protein, wherein said normal variant of said hcAMP-GEFII protein exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.

4. (Twice Amended) An isolated nucleic acid as in claim 2 wherein said nucleic acid encodes a normal variant of said hcAMP-GEFII protein, [and] wherein said nucleotide sequence comprises a sequence encoding a normal variant of said hcAMP-GEFII protein and capable of hybridizing under stringent hybridization conditions to a sequence complementary to a sequence encoding a protein comprising the human cAMP-GEFII amino acid sequence of SEQ ID NO: 18, and wherein said stringent hybridization conditions comprise a temperature between about 20°C and about 65°C and an ionic strength between about 5x SSC and about 0.1x SSC.

9. (Twice Amended) An isolated nucleic acid comprising a nucleotide sequence encoding at least one functional domain of an hcAMP-GEF II protein having the amino acid sequence of SEQ ID NO. 18; a normal variant of said hcAMP-GEFII protein, or a mutant of said hcAMP-GEFII protein, wherein said normal variant of said hcAMP-GEFII protein exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.

11. (Twice Amended) An isolated nucleic acid comprising a nucleotide sequence encoding an antigenic determinant of an hcAMP-GEFII protein (SEQ ID NO: 18) and selected from the group consisting of a normal variant of said hcAMP-GEFII protein, and a mutant of said hcAMP-GEFII protein, wherein said normal variant of said hcAMP-GEFII protein exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.

38. (Twice Amended) An isolated nucleic acid comprising a variant nucleotide sequence of a human cAMP-GEFII gene (SEQ ID NO: 17), said variant being selected from the group consisting of an allelic variant of said human cAMP-GEF II gene, and a heterospecific homologue of said human cAMP-GEFII gene, wherein said variant of said cAMP-GEFII gene encodes a protein that exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.

39. (Twice Amended) An isolated nucleic acid encoding a variant amino acid sequence of a human cAMP-GEFII protein (SEQ ID NO: 18), said variant being selected from the group consisting of an allelic variant of said human cAMP-GEF II protein, and a heterospecific homologue of said human cAMP-GEFII protein, and wherein said variant of said cAMP-GEFII protein exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.

42. (Amended) An isolated nucleic acid as in claim 41 wherein said expression vector may express said nucleotide sequence in mammalian cells in culture.

43. (Amended) An isolated nucleic acid as in claim 42 wherein said cells in culture are selected from the group consisting of fibroblast, liver, kidney, spleen, bone marrow, and neurological cells.

45. (Twice Amended) An isolated nucleic acid as in claim 41 wherein said expression vector encodes at least a functional domain of a protein selected from the group consisting of an hcAMP-GEFII protein having the amino acid sequence of SEQ ID NO: 18, a normal variant of said hcAMP-GEFII, and a mutant of said hcAMP-GEFII, wherein said normal variant of said hcAMP-GEFII protein exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.

50. (Twice Amended) A host cell in culture, said host cell comprising an expression vector of any one of claims 41-49, or a descendant thereof, wherein said host cell is transformed *in vitro* with said expression vector.

51. (Amended) A host cell in culture as in claim 50 wherein said host cell is selected from the group consisting of bacterial cells and yeast cells.

52. (Amended) A host cell in culture as in claim 50 wherein said host cell is selected from the group consisting of fetal cells, embryonic stem cells, zygotes, gametes, and germ line cells.

53. (Amended) A host cell in culture as in claim 50 wherein said cell is selected from the group consisting of fibroblast, liver, kidney, spleen, bone marrow and neurological cells.

54. (Amended) A host cell in culture as in claim 50 wherein said cell is an invertebrate cell.

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CLEAN COPY OF CLAIMS

1. (Canceled)

2. (Twice Amended) An isolated nucleic acid comprising a nucleotide sequence encoding a protein selected from the group consisting of an hcAMP-GEFII protein having the amino acid sequence of SEQ ID NO: 18, a normal variant of said hcAMP-GEFII protein, and a mutant of said hcAMP-GEFII protein, wherein said normal variant of said hcAMP-GEFII protein exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.

3. (Canceled)

4. (Twice Amended) An isolated nucleic acid as in claim 2 wherein said nucleic acid encodes a normal variant of said hcAMP-GEFII protein, wherein said nucleotide sequence comprises a sequence encoding a normal variant of said hcAMP-GEFII protein and capable of hybridizing under stringent hybridization conditions to a sequence complementary to a sequence encoding a protein comprising the human cAMP-GEFII amino acid sequence of SEQ ID NO: 18, and wherein said stringent hybridization conditions comprise a temperature between about 20°C and about 65°C and an ionic strength between about 5x SSC and about 0.1x SSC.

5. An isolated nucleic acid comprising a nucleotide sequence of at least 8 consecutive nucleotides selected from the group consisting of (a) nucleotides 1-2600 of SEQ ID NO. 17, and (b) a sequence complementary to nucleotides 1-2600 of SEQ ID NO. 17.

6. An isolated nucleic acid comprising a nucleotide sequence of at least 10 consecutive nucleotides selected from the group consisting of (a) nucleotides 1-2602 of SEQ ID NO. 17, and (b) a sequence complementary to nucleotides 1-2602 of SEQ ID NO: 17.

7. An isolated nucleic acid comprising a nucleotide sequence of at least 15 consecutive nucleotides selected from the group consisting of (a) nucleotides 1-2607 of SEQ ID NO. 17, and (b) a sequence complementary to nucleotides 1-2607 of SEQ ID NO. 17 .

8. (Canceled)

9. (Twice Amended) An isolated nucleic acid comprising a nucleotide sequence encoding at least one functional domain of an hcAMP-GEF II protein having the amino acid sequence of SEQ ID NO. 18; a normal variant of said hcAMP-GEFII protein, or a mutant of said hcAMP-GEFII protein, wherein said normal variant of said hcAMP-GEFII protein exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.

10. (Canceled)

11. (Twice Amended) An isolated nucleic acid comprising a nucleotide sequence encoding an antigenic determinant of an hcAMP-GEFII protein (SEQ ID NO: 18) and selected from the group consisting of a normal variant of said hcAMP-GEFII protein, and a mutant of said hcAMP-GEFII protein, wherein said normal variant of said hcAMP-GEFII protein exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.

38. (Twice Amended) An isolated nucleic acid comprising a variant nucleotide sequence of a human cAMP-GEFII gene (SEQ ID NO: 17), said variant being selected from the group consisting of an allelic variant of said human cAMP-GEF II gene, and a heterospecific homologue of said human cAMP-GEFII gene, wherein said variant of said cAMP-GEFII gene encodes a protein that exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.

39. (Twice Amended) An isolated nucleic acid encoding a variant amino acid sequence of a human cAMP-GEFII protein (SEQ ID NO: 18), said variant being selected from the group consisting of an allelic variant of said human cAMP-GEF II protein, and a heterospecific homologue of said human cAMP-GEFII protein, and wherein said variant of said cAMP-GEFII protein exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.

40. An isolated nucleic acid comprising a recombinant vector including a nucleotide sequence selected from the group consisting of SEQ ID NO: 17, and a sequence complementary to SEQ ID NO: 17.

41. An isolated nucleic acid as in claim 40 wherein said vector is an expression vector and said nucleotide sequence is operably joined to a regulatory region.

42. (Amended) An isolated nucleic acid as in claim 41 wherein said expression vector may express said nucleotide sequence in mammalian cells in culture.

43. (Amended) An isolated nucleic acid as in claim 42 wherein said cells in culture are selected from the group consisting of fibroblast, liver, kidney, spleen, bone marrow, and neurological cells.

44. An isolated nucleic acid as in claim 42 wherein said vector is selected from the group consisting of vaccinia virus, adenovirus, retrovirus, neurotropic viruses, and Herpes simplex.

45. (Twice Amended) An isolated nucleic acid as in claim 41 wherein said expression vector encodes at least a functional domain of a protein selected from the group consisting of an hcAMP-GEFII protein having the amino acid sequence of SEQ ID NO: 18, a normal variant of said hcAMP-GEFII, and a mutant of said hcAMP-GEFII, wherein said normal variant of said hcAMP-GEFII protein exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.

46. An isolated nucleic acid as in claim 41 wherein said vector further comprises sequences encoding an exogenous protein operably joined to said nucleotide sequence and whereby said vector encodes a fusion protein.

47. An isolated nucleic acid as in claim 46 wherein said exogenous protein is selected from the group consisting of lacZ, trpE, maltose-binding protein, poly-His tags, and glutathione-S-transferase.

48. An isolated nucleic acid comprising a recombinant expression vector including nucleotide sequences corresponding to an endogenous regulatory region of an hcAMP-GEFII gene (SEQ ID NO. 17).

49. An isolated nucleic acid as in claim 48 wherein said endogenous regulatory region is operably joined to a marker gene.

50. (Twice Amended) A host cell in culture, said host cell comprising an expression vector of any one of claims 41-49, or a descendant thereof, wherein said host cell is transformed *in vitro* with said expression vector.

51. (Amended) A host cell in culture as in claim 50 wherein said host cell is selected from the group consisting of bacterial cells and yeast cells.

52. (Amended) A host cell in culture as in claim 50 wherein said host cell is selected from the group consisting of fetal cells, embryonic stem cells, zygotes, gametes, and germ line cells.

53. (Amended) A host cell in culture as in claim 50 wherein said cell is selected from the group consisting of fibroblast, liver, kidney, spleen, bone marrow and neurological cells.

54. (Amended) A host cell in culture as in claim 50 wherein said cell is an invertebrate cell.

62. A method for producing at least a functional domain of an hcAMP-GEFII protein (SEQ ID NO: 18), said method comprising culturing a host cell of any of claims 50-54 under suitable conditions to produce said protein by expressing said nucleic acid.

118. (Canceled)

119. (Canceled)

120. (Canceled)